STARS increases skeletal muscle cell proliferation and differentiation

M.A. Wallace, S. Lamon and A.P. Russell, Centre for Physical Activity and Nutrition Research (C-PAN), School of Exercise and Nutrition Sciences, Deakin University, Burwood, VIC 3125, Australia.

Background and Aim: Skeletal muscle regeneration is dependent on the activation of satellite cells, the subsequent proliferation of myoblasts, followed by their myogenic differentiation and fusion with existing muscle fibres. Skeletal muscle cell proliferation and differentiation is controlled and coordinated by multiple signalling pathways and transcription factors. The striated muscle activator of rho signalling (STARS), a muscle specific actin binding protein, stimulates actin polymerization and influences serum response factor (SRF) transcription of genes involved in muscle cell growth, structure and function. The role of STARS in skeletal muscle cells is not well understood. Therefore, the aim of this study was to determine whether STARS regulated muscle cell proliferation and differentiation.

Methods: STARS was over-expressed in C2C12 myoblasts via a pFLAG-CMV4 mammalian expression plasmid containing the STARS mRNA sequence. Differences in cell proliferation were determined using DAPI staining (nuclei staining). In differentiating C2C12 myoblasts, STARS over-expression was achieved using adenoviral infection. C2C12 differentiation was assessed by measuring myotube fusion index via immunofluorescence and additionally by quantifying mRNA and protein expression of myogenic markers via real-time PCR and western blotting, respectively.

Results: STARS overexpression enhanced myoblast proliferation and was associated with increases in SRF target gene IL-6 and decreases in cell cycle regulators p21 and p27. STARS overexpression also enhanced myogenic differentiation and was associated with increased expression of differentiation markers muscle creatine kinase (Ckm), mitochondrial creatine kinase (Ckmt2) and myosin heavy chain. STARS overexpression increased the mRNA levels of several SRF target genes including α-actin and Mhc2b.

Conclusion: As STARS is a muscle specific protein that activates skeletal muscle cell proliferation and differentiation, it may be a future therapeutic target to enhance skeletal muscle repair and regeneration following damage.